

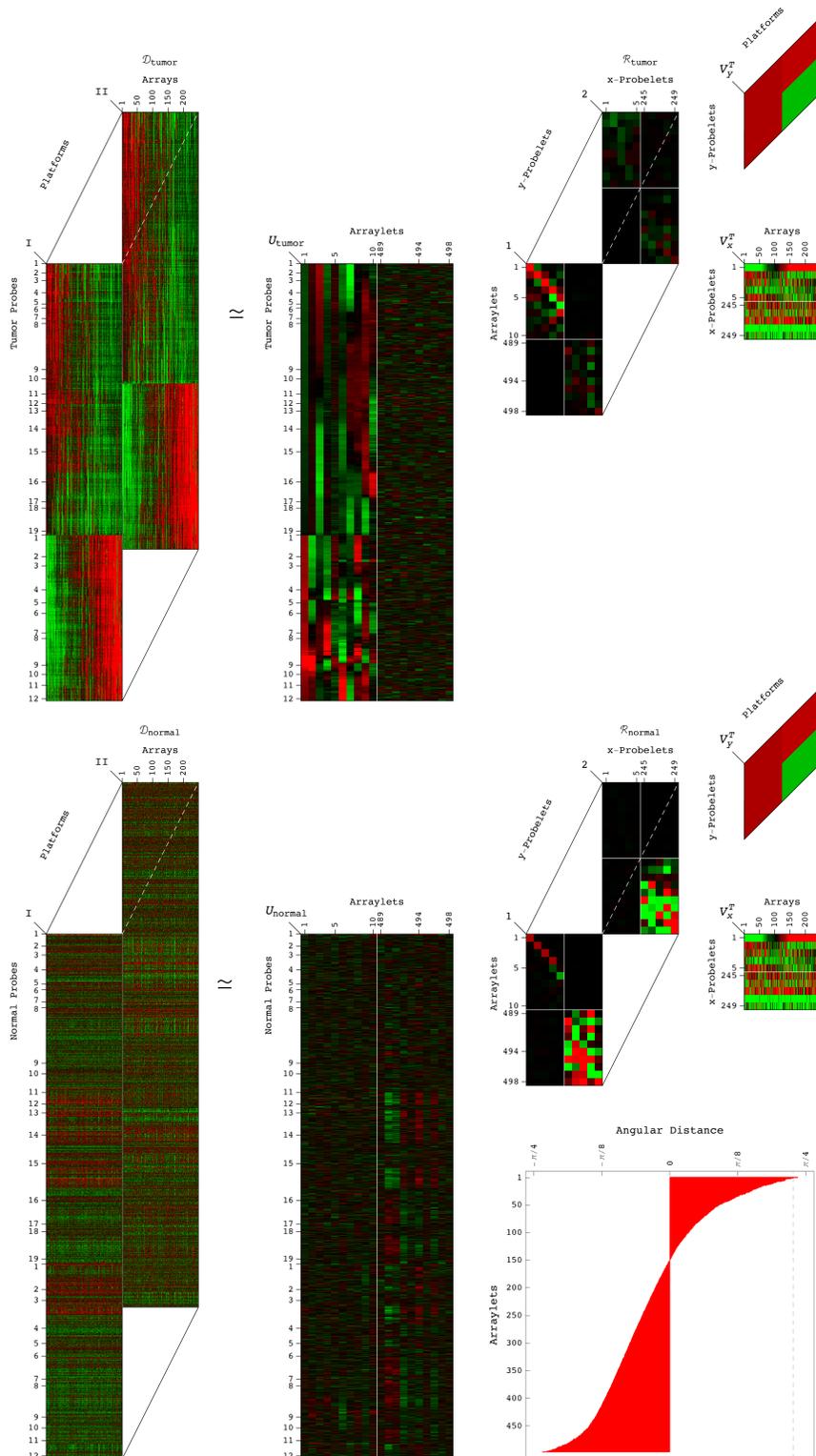
# A Novel Tensor GSVD Predicting Ovarian Serous Cystadenocarcinoma Survival and Response to Platinum-Based Chemotherapy

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## Introduction

The number of large-scale high-dimensional datasets recording different aspects of a single disease is growing, accompanied by a need for frameworks that can create one coherent model from multiple tensors of matched columns, e.g., patients and platforms, but independent rows, e.g., probes [1-3].



## Mathematical Framework: Tensor GSVD

We define and prove the mathematical properties of a novel tensor generalized singular value decomposition (GSVD), which can simultaneously find the similarities and dissimilarities, i.e., patterns of varying relative significance, between any two such tensors [4,5].

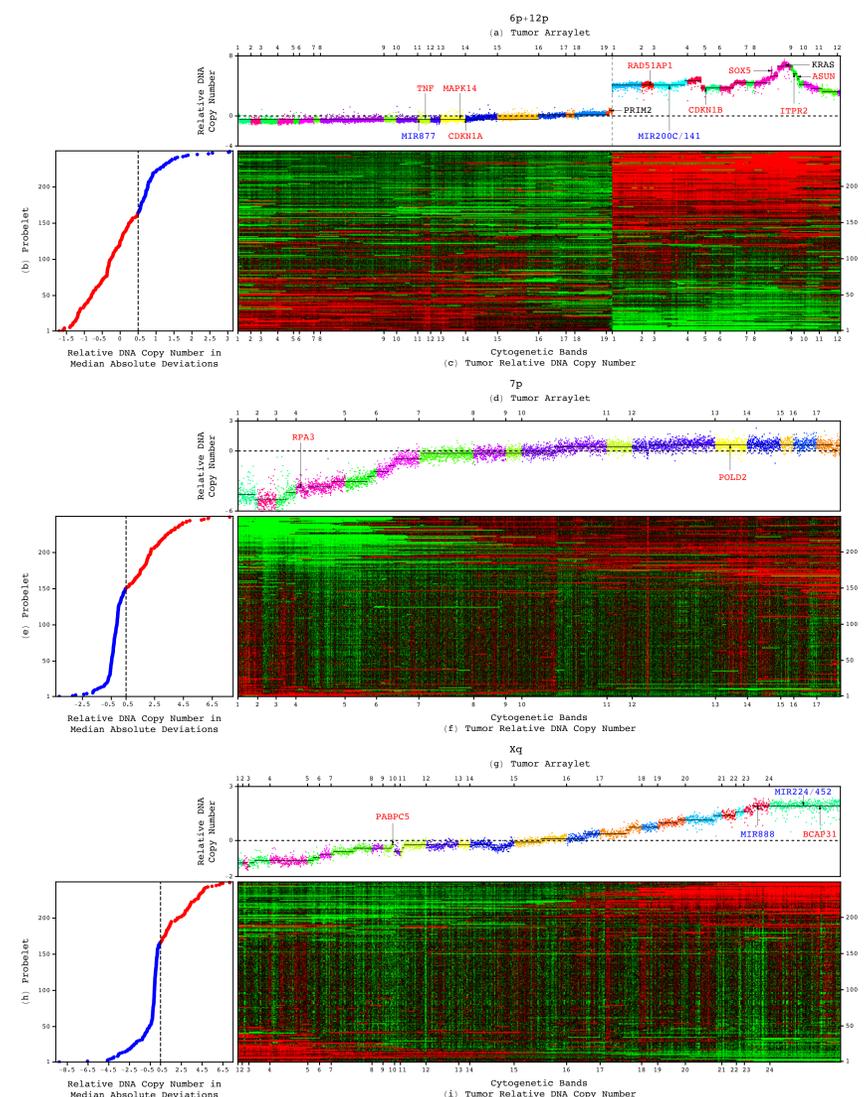
$$\mathcal{D}_i = \mathcal{R}_i \times_a U_i \times_b V_x \times_c V_y$$

$$= \sum_{a=1}^{LM} \sum_{b=1}^L \sum_{c=1}^M \mathcal{R}_{i,abc} \mathcal{S}_i(a, b, c),$$

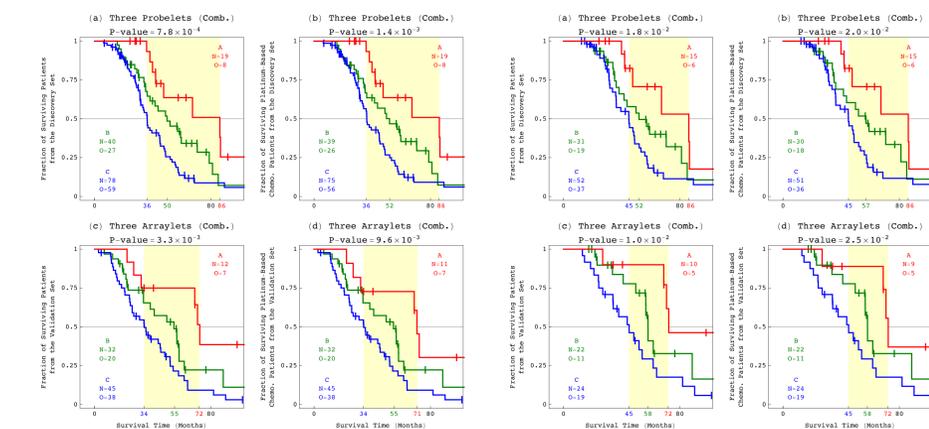
$$\mathcal{S}_i(a, b, c) = u_{i,a} \otimes v_{x,b}^T \otimes v_{y,c}^T \quad i = 1, 2.$$

## Biological Results

We demonstrated the tensor GSVD in comparative modeling of patient- and platform-matched but probe-independent ovarian serous cystadenocarcinoma (OV) tumor, mostly high-grade, and normal DNA copy-number profiles, across each chromosome arm, and combination of two arms, separately. The modeling uncovered previously unrecognized patterns of tumor-exclusive platform-consistent co-occurring copy-number alterations (CNAs) [6].



We found, first, and validated that each of the patterns across only 7p and Xq, and the combination of 6p+12p, is correlated with a patient's prognosis, is independent of the tumor's stage, and together with stage makes a better predictor than stage alone. The patterns can predict a patient's survival and response to platinum beyond the time of initial diagnosis, and throughout the disease, even in patients experiencing complete remission after the treatment of the primary tumor, and independent of the time interval to tumor recurrence or progression [7]. For >30 years prior, the best predictor of OV survival at the time of initial diagnosis was the tumor's stage. About 25% of primary OV tumors are resistant to platinum therapy, the first-line treatment, yet no diagnostic existed to distinguish resistant from sensitive tumors before the treatment.



Second, these patterns include most known OV-associated CNAs that map to these chromosome arms, as well as several previously unreported, yet frequent focal CNAs. Third, differential mRNA, microRNA, and protein expression consistently map to the DNA CNAs. A coherent picture emerges for each pattern, suggesting roles for the CNAs in OV pathogenesis and personalized therapy. In 6p+12p, deletion of the p21-encoding *CDKN1A* and p38-encoding *MAPK14* and amplification of *RAD51AP1* and *KRAS* encode for human cell transformation, and are correlated with a cell's immortality, and a patient's shorter survival time. In 7p, *RPA3* deletion and *POLD2* amplification are correlated with DNA stability, and a longer survival. In Xq, *PABPC5* deletion and *BCAP31* amplification are correlated with a cellular immune response, and a longer survival.

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